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LETTERS TO THE EDITOR

Anemia and Poor Prognosis in Advanced Heart Failure

I read with great interest the study by Horwich et al. (1) on the association of anemia with poor prognosis in advanced heart failure. The investigators observed that mortality decreased in linear fashion as hemoglobin level increased without excess mortality at the highest hemoglobin level. However, hemoglobin level >17 g/dl was seen in only 3% of men and 1% of women. Thus, the small number of patients at high hemoglobin level could have limited the investigators' ability to observe a U-shaped relationship.

The percentage of patients with chronic obstructive lung disease who are the most likely candidates to have high hemoglobin were not listed in the report. I would appreciate the investigators' comments.

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REPLY

We appreciate Dr. Ghali's interest in our recent investigation of the relationship between hemoglobin (Hb) level and mortality in patients with advanced heart failure (HF) (1). We fully agree with Dr. Ghali that our ability to detect excess mortality in HF patients with above-normal Hb levels is limited by the small number of patients in this population. The issue of optimal Hb levels in HF and the possibility of a U-shaped relationship with regard to mortality is increasingly important, as interest grows in correcting anemia in HF using erythropoietin or newer analogues.

Prospective epidemiological studies such as the Framingham Heart Study have demonstrated a U-shaped relationship between hematocrit and mortality due to cardiovascular disease (2). A preliminary analysis of elderly patients with mild to moderate HF enrolled in the Evaluation of Losartan In The Elderly (ELITE) II study showed a U-shaped relationship, with higher mortality seen in men with hemoglobin levels >16.5 g/dl and in women with hemoglobin levels >15.5 g/dl (3). It is interesting to note, however, that an analysis of patients with mild to moderate HF in the Studies Of Left Ventricular Dysfunction (SOLVD) database failed to find a U-shaped relationship between hematocrit and mortality in HF (4). Male patients with a hematocrit of 40% to 49% (n = 4,235) had a mortality rate similar to those with hematocrit levels above 50% (n = 344).

As Dr. Ghali points out, the highest Hb level would be expected in patients with severe chronic obstructive pulmonary disease (COPD). Unfortunately, we do not have data on rates of COPD in our cohort, as it was not a variable in our original study design. In our study and the analysis of the SOLVD database, only a small proportion of patients with HF had elevated hemoglobin or hematocrit levels. Analyses of HF populations that include patients with increased Hb levels secondary to COPD, congenital heart disease, or polycythemia vera would make assigning relative mortality risk of elevated Hb versus the primary disease process leading to increased hemoglobin extremely difficult.

Initial reports on using erythropoietin in mild to moderately anemic HF patients in order to raise Hb to at least 12.5 g/dl have shown clinical benefit and no adverse effects (5). Conversely, a randomized controlled trial in 1,233 patients with HF or ischemic heart disease along with renal failure on hemodialysis showed a trend for increased cardiovascular events in subjects randomized to maintain a hemoglobin of 14 g/dl compared to those with a goal of 10 g/dl (6). Further clinical trials are needed to definitively assess whether raising hemoglobin is beneficial in HF and whether there is an upper limit of hemoglobin level above which benefit is lost.

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Use of Term "Non-Q Infarction" is Questioned

The recent study in *JACC* titled "Revisiting the Culprit Lesion in Non–Q-Wave Myocardial Infarction" warrants comment (1). The

term "non-Q infarction," so common in today's literature, represents sloppy thinking and sloppy science. Infarcts due to circumflex disease may be very large and occasionally fatal and almost never cause Q-waves. Significant anterior wall infarction often reduces R-wave amplitude without resulting in Q-waves. The statement that non–Q-wave infarcts are different from those with Q-waves is using terminology that misrepresents the pathology. The viewpoint article by Phibbs and colleagues (2), reviewing this issue in detail three years ago in *JACC*, should be required reading. The editorial staff can discourage the use of this term by insisting that researchers who are ignorant of the pathology of infarction read the article by Phibbs et al.

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2. Phibbs B, Marcus F, Marriott HJC, Moss AJ. Q-wave versus non–Q-wave myocardial infarction: a meaningless distinction. J Am Coll Cardiol 1999;33:576–82.

REPLY

Dr. Ellestad assails our recent publication (1) on the angiographic findings that characterize the "culprit lesion" in patients with acute non–Q-wave myocardial infarction (MI) as representing "sloppy thinking and sloppy science." We presume this contentious allegation is directed toward our use of the term "non–Q-wave MI," which, along with the comparator term "Q-wave MI," is abhorred by Dr. Ellestad and others (2) who contend that this binary classification system "misrepresents the pathology" of MI and has been termed variably as "a halfway house of the intellect" (3), as having "no basis in scientific fact" (3), and as being "a meaningless distinction" (2). Such pemicious rhetoric serves only to discredit the stature and integrity of the physician assailants and to reinforce the belief that such strong contrarian views are discordant with mainstream cardiology opinion and practice.

At the time that the VANQWISH trial was conducted (1993 to 1996) and reported (1998) (4), the accepted terminology promulgated by both major national cardiology organizations (American College of Cardiology and American Heart Association) consistently endorsed the terms "Q-wave" and "non–Q-wave" MI in their Consensus Management Guidelines (5), suggesting that subject-matter experts and opinion leaders in cardiology did not consider such concepts and terms meaningless or irrelevant.

More recently, of course, the older nomenclature of "Q-wave" and "non–Q-wave" MI has been replaced by a new binary classification system ("ST-segment elevation" and "non–ST-segment elevation" MI), but because our current study was undertaken in an era when the former classification was both widely accepted and used, we decided for the sake of consistency to use the term "non–Q-wave" MI rather than "non–ST-segment elevation" MI in reference to our recent coronary angiographic substudy (1).

We lament Dr. Ellestad's uncritical assertion that both the *JACC* editorial staff and the VANQWISH investigators are "ignorant of the pathology of infarction." We are all well aware of the important distinction by which total or subtotal occlusion of the circumflex or obtuse marginal branch coronary circulation can "masquerade" as "non–Q-wave" MI; in fact, we were the first to document (in 1987) the early electrographic findings of true posterior MI (6), based on our careful and comprehensive assessment of serial electrocardiograms (ECGs) in the Diltiazem Reinfarction Trial (7). Moreover, we have contributed significantly to the cardiology literature regarding the important electrocardiographic features of non–Q-wave (non–ST-segment elevation) MI, (8–10) and obviously incorporated these same rigorous criteria for use in the VANQWISH study (4), which, we believe, permitted us to accurately and reliably exclude posterior MI from our study population.

Although our views are unlikely to dissuade Dr. Ellestad and the vocal minority of cardiologists who tenaciously adhere to the holistic notion that "an infarct is an infarct" electrocardiographically, pathogenetically, clinically, angiographically, and prognostically—a view, unfortunately, that ignores and disdains an abundance of scientific information that has been acquired and assimilated over more than 25 years of careful study—we hope that our recent report on the angiographic characteristics of "culprit lesions" will aid more cognitive cardiologists to focus on ways of optimizing the care and management of their patients with non–Q-wave/non–ST-segment elevation MI rather than getting "lost among the forest and trees" of a largely outmoded terminology battle that is of little relevance to contemporary clinical practice.

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